PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 30 January 2001 (30.01.01)	
International application No. PCT/EP00/05632	**Applicant's or agent's file reference** 53 123 V
International filing date (day/month/year) 19 June 2000 (19.06.00)	**Priority date** (day/month/year) 18 June 1999 (18.06.99)
Applicant FRITZ, Eberhard et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

06 December 2000 (06.12.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer R. E. Stoffel
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
53 123 V		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 00/ 05632	19/06/2000	18/06/1999
Applicant		
AEA TECHNOLOGY QSA GMBH		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [ ] as suggested by the applicant.

   [X] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

16

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
53 123 V		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/05632	19/06/2000	18/06/1999
International Patent Classification (IPC) or national classification and IPC A61N5/10		
Applicant AEA TECHNOLOGY QSA GMBH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06/12/2000	24.08.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Böttcher, S Telephone No. +49 89 2399 2875

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/05632

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-17 as originally filed

Claims, No.:

1-22 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 17-22.

because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 17-22.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

   Novelty (N) Yes: Claims 4, 5, 8, 15

	No:	Claims	1-3, 6, 7, 9-14, 16
Inventive step (IS)	Yes:	Claims	
	No:	Claims	4, 5, 8, 15
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:
   D1: WO-A-97 18012
   D2: US-A-5 833 593

2. The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses:

   A radiation source for use in endovascular radiation treatment which comprises one or more treating elements (196') comprising a radiation emitting element (206') and means for containment of said radiation emitting element (198'), wherein said treating elements are comprised in an elongated container ("sleeve") having at least one deflection site (see figs. 36A and 37A; and page 3, lines 11-15 and lines 26-28; and page 36, line 32 - page 37, line 8).

   Hence, the subject-matter of claim 1 lacks novelty over document D1 (Art. 33(2) PCT.

3. Dependent claims 2-16 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, the reasons being as follows:

3.1 The features of dependent claims 2, 3, 6, 7, 9-14 and 16 are also known from document D1 (see page 24, lines 3-5, page 27, line 37 - page 28, line 3 and page 35, line 36 - page 37, line 17). The subject-matter of these claims therefore lacks novelty, too.

3.2 In claims 4, 5, 8 and 15 slight constructional changes in the radiation source of claim 1 are defined which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims lacks an inventive step (Art. 33(3) PCT).

3.3 The optional and "preferred" features included in claims 3, 7, 11 and 12 also represent obvious design modifications and, therefore, do not involve an inventive step either.

4. Attention is drawn to the fact that document D2 also discloses all the features of claim 1 and of dependent claims 2, 3, 6, 9-13 and 16 (see column 7, line 12 - column 9, line 8, column 10, lines 16-36 and column 11, lines 13-56).

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
EP-A-0 993 843	19.04.2000	13.10.1999	14.10.1998

The document is considered to anticipate the subject-matter of independent claim 1.

Re Item VIII

Certain observations on the international application

With the bracketed expression "(seeds)" in claims 1 and 12 a lack of clarity (Art. 6 PCT) arises because it is not clear whether this feature is optional or not.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
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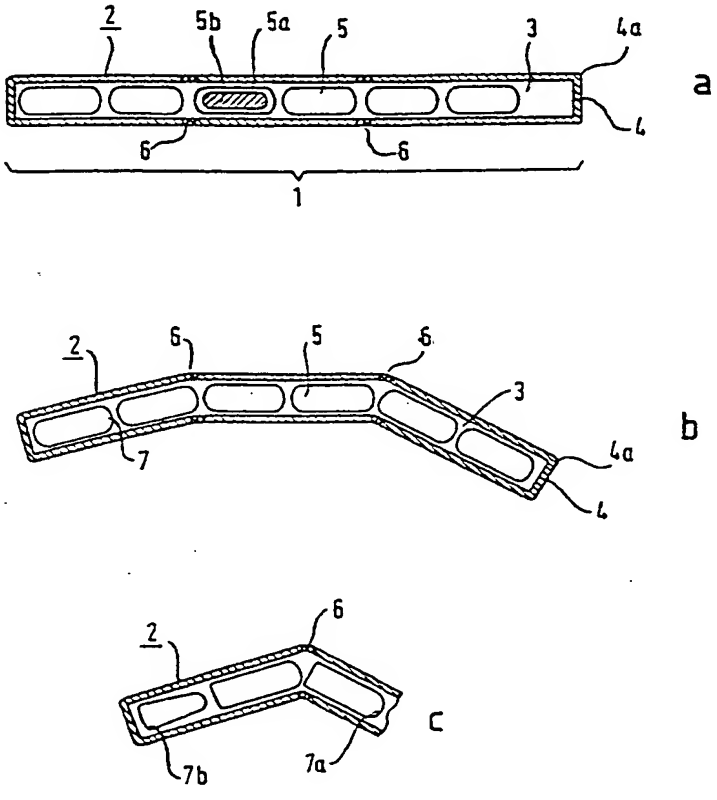
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: RADIATION SOURCE FOR ENDOVASCULAR RADIATION TREATMENT



(57) Abstract: According to the invention there is provided a radiation source for use in endovascular radiation treatment which comprises one or more and preferably at least two treating elements or seeds comprising a radiation emitting element and means for containment of said radiation emitting element which radiation source is characterized in that said seeds comprised in an elongated container having at least one deflection site. There is further provided an apparatus for endovascular radiation treatment comprising an elongaged catheter, optionally a guide wire and the radiation source as defined above. According to another aspect there is provided a method for endovascular radiation treatment comprising the steps of directing an elongated catheter to the selected site to be treated, introducing a radiation source as defined above into the catheter at its proximal end portion, moving said radiation source to the distal end portion of the catheter preferably by use of a transfer wire, maintaining said radiation source at that distal end portion for a predetermined period of time and retracting said radiation source to the proximal end portion of the catheter preferably by use of a transfer wire.

WO 00/78395 A1

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Radiation Source for Endovascular Radiation Treatment

The present invention relates to a radiation source for use in endovascular radiation treatment which radiation source comprises radiation emitting elements and is suitable for being delivered in a catheter to the selected site to be treated within the vascular system of a patient. The invention further relates to an apparatus for vascular radiation treatment using said radiation source as well as a method of treatment.

BACKGROUND OF THE INVENTION

Endovascular radiation treatment is the todays method of choice to prevent formation of scar tissue in a blood vessel which has been injured in various ways, for example, as trauma from surgical or diagnostic procedures. One area of the vascular system of particular concerns with respect to such injury is coronary arteries that are subjected to procedures for removing or reducing blockages due to plaque within the arteries. Partial and even complete blockage of the coronary arteries by the formation of an arteriosclerotic plaque is well known and a serious medical problem. Such blockages may be treated using arterectomy devices which mechanically remove the plaque, hot or cold lasers which vaporize the plaque, stents which hold the artery open and other devices and procedures well known in the art. The most common of them is the percutaneous transluminal coronary angioplasty, more commonly referred to as balloon angioplasty.

In this procedure a catheter having an inflatable balloon at its distal end is introduced into the coronary artery, the uninflated balloon is positioned at a stenotic site and the balloon is inflated. Inflation of the balloon disrupts and flattens the plaque against the arterial wall and stretches the arterial wall, resulting in enlargement of the intraluminal passageway and increased bloodflow. After such extension, the balloon is deflated and the balloon catheter removed.

Long term success of balloon angioplasty procedures is largely limited due to restenosis or re-closing of the intraluminal passageway through the artery by formation of scar tissue. Restenosis is experienced in approximately 30 to 50 % of the patients within six months after balloon angioplasty. Apparently restenosis is to a significant extend a natural healing response to the vessel injury caused by inflation of the angioplasty balloon.

Such injury of the vessel typically initiates the bodies own natural repair and healing process. During the healing process, fibrin and plathelets rapidly accumulate in the endothelium and vascular smooth muscle cells proliferate and migrate into the intima. The formation of scar tissue by smooth muscle proliferation (hyperplasia) is believed to be a major contributor to restenosis following balloon angioplasty of the coronary artery.

Prior attempts to inhibit restenosis have included the use of various light therapies, chemotherapeutical agents, stents, arterectomy devices, hot and cold lasers and so on. The most promising approach to inhibit restenosis is the use of endovascular radiation therapy, i.e. the exposure of the restenotic site to ionizing or radioactive radiation.

Although endovascular radiation therapy in general has been applied advantageously, the devices available for delivery of radiation sources and the radiation sources themselves have certain drawbacks which limit their usefulness. Typically, the devices include a catheter, which is directed by way of a guide wire inserted therein to the site of treatment. The catheter is then used to internally direct the radiation source to the site of treatment.

One typical problem encountered with the catheter and/or the radiation source is related to stiffness of the source which is mostly directly proportional to its length. Thus shorter radiation sources are typically used to allow them to follow the bends of the artery. To irradiate the entire site of the vessel to be treated a so-called "stepping-treatment" is then employed, wherein the radiation source is moved back and forth in the vessel. Since, however, exact positioning is not possible in a constantly moving vessel, irradiation is not precisely controllable in this "stepping-treatment". Thus, long sources are desirable which allow for one-step treatment of the site in its entire length.

For example, US-A-5,833,593 discloses a flexible source wire which is modified at its treatment end to receive a radioactive element. A plug seals the unmodified section of the source from the lumen of the modified segment or container which contains the radioactive element. Both ends of the source wire are sealed to prevent leakage of radioactivity. The source wire is then inserted in a catheter for guiding the same to the treatment site. The modified section or container itself is rigid and is only flexibly linked to the remainder, unmodified portion of the source.

From US-A-5,683,345 an apparatus and a method are known which apparatus includes an elongated flexible catheter tube having proximal and distal end portions with one or more lumina extending therebetween. One or more treating elements or seeds containing radioactive material are positionable within the first lumen and are movable between the proximal and distal end portions under the force of liquid flowing through the lumina. The radiation source used according this document consists of individual treating elements which may be joined together to form a train of treating elements by use of several length of high tempered spring wire to prevent the treating elements from becoming too spaced apart while moving through the catheter.

Other typical drawbacks encountered with prior art radiation sources and devices for delivering the same to the site to be treated are related to the duration of exposure, controllability of the radiation exposure (dosage, homogeneity of treatment), the necessity to conduct a "stepping-treatment", or difficulties in completely and controllably retracting the radiation source from the catheter and therefore the risk of undesirable exposure of both the patient and any medical personal handling the treatment device. It is the object of the invention to overcome these and other drawbacks of prior art radiation sources.

SUMMARY OF THE INVENTION

This object is solved by the radiation source of the invention as disclosed in the appended claims.

In a first aspect the invention relates to a radiation source for use in endovascular radiation treatment which comprises one or more, preferably at least two treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element, wherein said seeds are comprised in an elongated container having at least one deflection site.

According to a preferred embodiment the elongated container is made from a highly flexible material such as plastics, rubber, or a memory resistant material such as a Ni-Ti-alloy or an aluminum alloy, more preferably Nitinol or Tinal alloy BB.

According to a preferred embodiment, the elongated container is a hollow cylinder or tube preferably having end caps or plugs to close the same. Preferably these end caps are rounded end caps to allow for easy movement of the container.

Preferably the one or more deflection site(s) comprise perforation patterns, preferably laser perforations of the container. These perforations may be arranged in a belt around the same. The one or more deflection site(s) may also comprise multiple helical openings in the container, which as well may be arranged in a belt around the elongated container.

Preferably the seeds comprise spherical or rounded end caps on one or both ends. They may be separated from each other by interdisposing at least one spacer, preferably in form of a sphere therebetween.

According to another embodiment the seeds are spaced from each other and fixed to the inner wall of the container, preferably by way of point welding.

In another aspect the invention relates to an apparatus for endovascular radiation treatment, comprising (1) an elongated catheter having a proximal end portion and a distal end portion, a lumen extending therebetween for receiving a radiation source, (2) optionally a guide wire and a second lumen therefore, and (3) a radiation source which comprises one or more and preferably at least two treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element,

wherein said seeds are comprised within an elongated container having at least one deflection site.

Preferably the apparatus comprises a x-ray fluoroscopy device for monitoring the radiation source.

In another embodiment the apparatus may comprise a magnetic means for guiding the radiation source. In this case the elongated container is preferably made from a magnetic material such as Fe or an Fe-alloy.

Preferably the apparatus may also comprise a containment vessel for storage of the elongated container and/or the individual seeds. The containment vessel can be in flow communication with the catheter lumen and/or can be a separate or separable device for separate storage and/or disposal.

In a preferred embodiment the container is linked to a transfer wire for moving the same in a catheter. Such linkage may be flexible or rigid and is preferably made at the proximal end portion of the elongated container. The transfer wire may also comprise an extension of the container itself.

In a third aspect the invention relates to a method for endovascular radiation treatment, comprising the steps of

(a) directing an elongated catheter having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, to the selected site to be treated preferably by way of a guide wire in a separate lumen,

(b) introducing a radiation source into the catheter at its proximal end portion, which radiation source comprises one or more, preferably at least two treating elements (seeds) and wherein said seeds are comprised within an elongated container having at least one deflection site,

(c) moving said radiation source to said distal end portion of the catheter preferably by use of a transfer wire,

(d) maintaining said radiation source at said distal end portion for a determined period of time, and

(e) retracting said radiation source to the distal end portion preferably by use of a transfer wire.

Preferably moving and/or retracting in steps of (c) and/or (e) is achieved by pushing or pulling the radiation source. According to a preferred embodiment the seeds are comprised in a magnetic elongated container and the transfer wire comprises a magnet to magnetically effect said pulling of the radiation source in steps (c) and/or (e), more preferably the transfer wire itself is magnetic.

In an alternative embodiment an external magnet field may be applied to move the radiation source comprising the seeds within a magnetic elongated container by magnetic forces.

According to another embodiment movement in step (c) is achieved by pushing and movement in step (e) is achieved by pulling the elongated container using a transfer wire linked to the container at its proximal end portion.

SHORT DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic view of the radiation source according to the invention in straight (Fig. 1a) and bent (Fig. 1 b) position, Fig. 1c showing various forms of the seeds to be used.

Fig. 2 is a schematic drawing of a radiation source according to the invention comprising spheres as spacers between the seeds to form internal joints.

Fig. 3 is a schematic drawing of a radiation source according to the invention, wherein the seeds are spaced apart from each other and are fixed to the inner wall of the container by point welding.

Fig. 4 is a schematic drawing of a radiation source according to the invention wherein the deflection site of the container is formed e.g. by laser perforations.

Fig. 5 is a schematic drawing of the container according to the present invention, wherein the deflection site is formed by helical openings in the container.

Fig. 6 is a schematic drawing of the catheter of the present invention.

In the above figures like reference numerals indicate like parts of the radiation source.

DETAILED DISCLOSURE OF THE INVENTION

In the following the invention will more in detail be disclosed and illustrated by way of reference to accompanying drawings. Radiation in the sense of the application is to be understood as ionizing or radioactive radiation.

The radiation source for use in endovascular radiation treatment according to the invention comprises one or more, preferably at least two treating elements, so-called seeds. These seeds comprise a radiation emitting element or radiation emitting core and a means for containment of said radiation emitting element. The radiation source of the invention is characterized in that the seeds are comprised in an elongated container having at least one deflection site. Held together in the container the seeds form an elongated flexible radiation source of the desired length which length is determined by the length of the container chosen.

The expression "container" relates to any means capable of receiving and holding together the seeds, although the seeds need not necessarily be directly attached or linked to each other.

The expression "deflection site" refers to a site at which at least one deflection part of the elongated container can be made to deviate from the longitudinal axis thereof, typically by bending the same. Bending may be accomplished by some type of joint, formed internally or externally, or merely due to flexibility of the container material itself.

The expression "elongated" is used herein to indicate that the container has longitudinal axis larger than its height or depth. It is to be understood that the shape of the container can be chosen freely provided it meets the above requirement of being "elongated" and further provided its shape does not interfere with its movement in a catheter. Typically the container will thus have a circular cross-section, but may also have cross-sections of irregular, elliptic, rectangular, hexagonal, octagonal etc. form.

Preferably the container is in form of a hollow cylinder or tube preferably having end-plugs or end caps, preferably rounded (no sharp edges), at both ends to close the same. However, the container needs not necessarily be tightly closed, but may be comprised of a mesh, or a woven or non-woven material, provided this material allows to hold the seeds together within the form of the container and equally allows for providing deflection sites therein.

The container may be made from any suitable material which is sufficiently resistant against irradiation, permits transmission of radiation therethrough and allows for formation of deflection sites. Preferably the container is made from a flexible material such as plastics, thermoplastic resins, acrylics, rubber or from a memory-resistant material such as Ni-Ti-alloys e.g. Nitinol or aluminum alloys such as Tinal alloy BB. In a preferred embodiment the container is a hollow cylinder made of Nitinol and comprises rounded end caps made from the same material.

According to another embodiment the container may be made from or may comprise a metallic material which may either be a magnetic or a magnetizable material such as steel, stainless steel, Co, Ni, Fe, Mn, ferrites Ag, Pb, Co, Cr, Nb or their alloys, which magnetizable material can be magnetized by applying an external magnetic field.

The elongated container may comprise a coating layer which allows for reducing friction to improve movement of the elongated container within the catheter. This coating may be for example of teflon material or a similar low-friction material to reduce friction between the elongated container and the internal wall of the catheter in which it moves.

In case the container is made from a flexible material itself or from a mesh, a woven or non-woven web, deflection sites are constituted by appropriate choice of material of the container.

According to a preferred embodiment, the one or more deflection site(s) comprise perforation patterns, preferably laser perforations of the elongated container which are preferably arranged in a belt around the container at an appropriate site to form a deflection site. The one or more deflection site(s) may equally comprise multiple helical openings in the container. These are again arranged appropriately in a belt around the container at the suitable site.

Preferably the one or more deflection sites are arranged such that each is located exactly over the portion of the internal lumen of the container, where two end caps of seeds are opposingly faced to each other.

In a preferred embodiment the seeds comprise rounded, preferably spherical end caps on one or both sides thereof. These rounded or spherical end caps may function as internal joints. According to another embodiment the seeds are separated from each other by at least one spacer, preferably in form of a sphere preferably having about the same diameter as the seeds. This sphere may function as an internal joint. In this embodiment the seeds need not necessarily comprise rounded or spherical end caps, but may have flat end caps as well. The seeds may be spaced apart by two or more spheres interdispersed therebetween, but preferably are separated by only one sphere. The spacer itself is limited with its diameter by the internal diameter of the container and may have a smaller diameter than the seeds, provided it still sufficiently functions as an internal joint.

According to another embodiment the seeds are spaced apart from each other and are fixed to the internal wall of the elongated container to held them spaced apart and to thereby allow for providing an internal deflection site of the container. Preferably fixing of the seeds is made by point welding.

The internal diameter of the container must be sufficient to slidably receive the seeds with their means for containment typically having an outer diameter of between 0.2 and 0.8 mm. As regards the longitudinal dimension, i.e. the internal length of the lumen of the elongated container, this must be sufficient to receive the one or more, preferably at least two seeds and is preferably sufficient to receive a sufficient number of seeds to provide a radiation source of the desired length.

The internal lumen of the container may be evacuated, may comprise a gas or may comprise any suitable liquid, such as sterilized water, phosphate buffered saline, a saline solution, any inert hydrocarbon etc. provided its filling does not interfere with radiation treatment.

The outer diameter of the elongated container is as to the lower limit limited by the internal diameter thereof and is on the other hand small enough to slidably fit in a catheter and a blood vessel to be treated. Preferably such diameter is in the range of above about 0.3 to about 1 mm.

The radiation source of the present invention comprises one or more, preferably at least two treating elements or seeds. Typically the number of seeds comprised in this radiation source is chosen to cover the desired length of the vessel to be treated. Preferably the radiation source will cover a number of seeds sufficient to provide a radiation source of at least 4 mm in length, preferably 10 to 50 mm in length, more preferably 20 to 40 mm in length. The length of the elongated container is chosen appropriate thereto.

Typically the individual seeds will have a length in the range of 1.0 to 10.0 mm, more preferably 1.5 to 4.0 mm and most preferred 2.0 to 3.0 mm. Preferably the seeds are of

tubular shape and have an outer diameter of the means of containment thereof in the range of between 0.2 and 1.0 mm, preferably between 0.2 and 0.8 mm.

The means for containment typically is a capsule. This capsule may be elongated, and may be a hollow cylinder or tube comprising a first and a second end plug, but may have any shape suitable for forming seeds such as spheres. ellipsoids, doughnuts, cones, flat-end-tubes, disks, cubes etc.; provided it comprises a cavity for receiving and enclosing said radiation emitting element.

Preferably the means for containment is a metallic capsule which is, for example, made from a metal selected from the group comprising stainless steel, Ag, Pt, Ti, Ni, Fe, Mn, Cr, Nb, Co, Au or their alloys, including mixtures thereof. More preferably the means for containment, i.e. the seed comprises rounded or spherical end caps on one or both ends, which end caps may also form the above first and second end plug. The means for containment may also be formed from glass or plastics material such acrylics e.g. by coating a solid radiation emitting element to obtain a tight coating layer, provided it prevents leakage of radioactivity in the lumen of the catheter. It may further comprise a coating e.g. of teflon material or a similar low-friction material to reduce friction between the treating element or seed and the inner wall of the container.

The radiation emitting element comprised in that means for containment comprises any α-, β- and/or γ-emitting substance, preferably a pure β-particle emitter or a β- and γ-emitting substance. Typically the radiation emitting element comprises one or more radioactive materials selected from the group comprising Cs^{137}, Co^{57}, Sr^{89}, Y^{90}, Au^{198}, Pd^{103}, Se^{75}, Sr^{90}, Ru^{106}, P^{32}, Ir^{192}, Re^{188}, W^{188} and I^{125}.

The radioactive material may be contained in a solid such as metal, glass, foil or ceramics or in a free flowing form such as a powder or liquid or is dispersed in a fluid. Neither form or state of the radioactive material is crucial, provided it allows for introducing the same in the means for containment and for secure containment.

The seeds are prepared by introducing the radiation emitting element into the means for containment and closing the same, e.g. by fixing the second end plug, e.g. by welding. The seeds may also be formed by coating an appropriately shaped ceramic radioactive core with a means for containment, e.g. by dipping the core in a coating solution, sputtering etc. The entire radiation source is then prepared by introducing the desired number of seeds into the elongated container previously prepared by known techniques and closing the same, if desired.

The amount of radioactivity is typically in the range of 0.45 to 25,000 mCi per centimeter of vessel to be treated, depending on the radiation source used. The emitted radiation should be sufficient to deliver a desired dosage of from 100 to about 10,000 rads, preferably about 700 to 5,000 rads in a about 2 to 10 minutes to the tissue to be treated.

The elongated radiation source as shown in Fig. 1 comprises an elongated container (1) comprising a hollow tube (2) and flat end plugs (4) having rounded edges (4a). The internal lumen (3) of the container is adapted to receive several seeds (5) comprising a means for containment (5a) and a radiation emitting element (5b). The hollow tube of the container further comprises deflection sites (6). As can be seen from Fig. 1 and 1a, the deflection sites (6) are located at a region of the tube where internally the spherical or rounded end caps (7) of two seeds (5) are opposingly faced to each other. Thereby, the spherical end caps function as internal joints to support bending of the deflection site(s). Further, the end caps allow for homogenous three-dimensional distribution of radiation from the seed so that bending of the radiation emitting source or the container does not result in inhomogenities of irradiation of the surrounding tissue.

Fig. 1c shows various types of seeds with spherical (7a) or rounded (7b) end caps, which can be used in the radiation source of the invention.

According to another preferred embodiment as shown in Fig. 2, the individual seeds (5) as comprised within the container lumen (3) are spaced apart from each other by interdisposed spheres (8). These spacers in the form of spheres need not comprise a radiation

emitting element or core but may be constituted of a neutral, non-radiation emitting material.

As shown in Fig. 2 the seeds (5) may comprise spherical end caps (7), but may also comprise flat ends having rounded edges (rounded end caps), since the one or more sphere(s) interdisposed between the seeds sufficiently support bending of the deflection sites (6) already. Again the deflection site (6) is suitably located in a position surrounding the interdisposed sphere (8) to create optimal a match with the internal deflection site of the elongated container (1).

According to another preferred embodiment as shown in Fig. 3 the seeds (5) comprised in the container lumen (3) are fixed to the internal wall of the elongated container (2) by way of point welding. Fixing may occur at one or more sites on the means of the containment (9) of the seed. Preferably the deflection sites (6) of the container (2) are arranged such that they match the gaps between the seeds fixed to the internal container wall.

As can be seen from Fig. 4 and Fig. 5, according to these preferred embodiments each of the one or more deflection site(s) of the container in the respective embodiments is constituted by a belt surrounding its outer diameter of a perforation pattern (10) or e.g. helical openings (11).

The radiation source of the invention comprising an elongated container having at least one deflection site and seeds held together in this container provides a radiation source which is movable by pushing or pulling the entire container. Such movement may be accomplished by use of a transfer wire which can be mechanically and/or magnetically linked to one end of the elongated container.

The invention thereby simplifies handling of the radiation source and avoids distribution of the seeds within the catheter lumen by chance. At the same time the length of the source is not limited by its stiffness or rigidity due to the at least one deflection site provided in the container. Thus, the radiation source of the invention allows for an

elongated source permitting a one-step radiation treatment of elongated segments of the vessel. Due to the one or more deflection site(s) provided in the elongated container of the radiation source of this invention, the radiation source can easily follow the bends and partitions of a blood vessel within the body to be treated.

Since the radiation source of the invention can be moved by pushing and pulling the radiation source of the invention can be used in a catheter comprising only one central lumen for receiving the source and optionally the transfer wire. Accordingly, the radiation source or its seed can be arranged in the central axis of the vessel to be treated to allow for a uniform and homogenous radiation of the surrounding tissue. This has to be considered an important aspect as radiation intensity decreases strongly with distance from the radiation source and an out of center location of the radiation source will result in unpredictable and non-controllable inhomogenities in the radiation field created therefrom. Thus, with an out of center arrangement of the radiation source inhomogeneous radiation of the surrounding tissue results. This is overcome by use of the present radiation source.

According to the present invention, there is further provided an apparatus for endovascular radiation treatment comprising (1) an elongated catheter having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, (2) optionally a guide wire in a separate lumen and (3) a radiation source as disclosed above.

Referring to Fig. 6 the apparatus of the invention makes use of a catheter (12) which is typically made from nylon material although other plastic material may be used as well. The outer diameter of the catheter is sized according to the intended application, e.g. 5 mm or smaller for use in treating the stenotic site of a coronary artery. The inner diameter of the lumen (14) extending between the distal end portion (13a) and the proximal end portion (13b) of the catheter is correspondingly sized to receive the elongated container and is typically in the range of from about 0.3 to about 1.0 mm. The catheter may not have sufficient strength or torsional rigidity for insertion along a lengthy serpentine vascular path and may then require use of a guide wire. This guide wire is then arranged in a separate lumen having in most cases a smaller diameter than the lumen for

receiving the radiation source. Typically angioplasty procedures result in a distance between the percutaneous entryport and the coronary artery of approximately 90 to 120 cm, the length of the catheter corresponding thereto. The lumen may internally have a coation for to reduce friction and/or may be filled with a suitable liquid such as mentioned above for the elongated container.

To assist in positioning the distal end portion (13a) of the catheter (12) at the desired location or site to be treated, the catheter may be advanced over a guide wire (not shown) that is preinserted to the desired location in the manner well known in the art. The guide wire is one commonly used in prior art and can be made from any type of metal, preferably memory-resistant metals, i.e. materials that can accept up to a 1 % strain with less than a 1 % permanent alteration in its original configuration. Preferred materials include nickel-titanium alloys such as Nitinol or aluminum alloys such as Tinal alloy BB. In the apparatus of the invention, a separate wire as above, the so-called transfer wire (16), is used for moving said radiation source. In the terms of the description a guide wire is used for directing the catheter, whereas a transfer wire is used for moving the radiation source.

The apparatus of the invention may further comprise a containment vessel for a storage of the radiation source and for shielding the patient to be treated and the medical personal from exposure from radiation during introduction and retraction of the catheter. The containment vessel preferably is in flow communication with the catheter, although it can be constructed as a separate and/or separable part to allow for separate storage and disposal.

The apparatus of the invention may further comprise a x-ray fluoroscopy device for monitoring the radiation source as, for example, described in US-A-5,833,593. This allows for exact positioning of the radiation source, which may in this case carry a marker on one or both ends, and thus allows for precise control of the treatment site.

Finally, the apparatus of the invention may comprise a magnetic means for guiding the radiation source in case the radiation source is created from a magnetic container.

In a third aspect there is provided a method for vascular radiation treatment comprising the steps of

(a) directing an elongated catheter having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, to the selected site to be treated preferably by way of a guide wire in a separate lumen,

(b) introducing a radiation source into the catheter at its proximal end portion, which radiation source comprises one or more, preferably at least two treating elements (seeds), said seeds comprising a radiation emitting element and means for containment of said radiation emitting element, and said seeds being comprised in an elongated container having at least one deflection site,

(c) moving said radiation source to said distal end portion preferably by use of a transfer wire,

(d) maintaining said radiation source at said distal end for a determined period of time, and

(e) retracting said radiation source to the proximal end portion preferably by use of a transfer wire.

Preferably a radiation source as above is used. The steps of moving and/or retracting (c) and/or (e) can be achieved by pushing or pulling the radiation source.

More in detail, according to one preferred embodiment, movement in step (c) is achieved by pushing and said movement or retracting in step (e) is achieved by pulling said radiation source. For doing so, the radiation source may be mechanically and/or magnetically linked to a transfer wire at its proximal end. In this embodiment the radiation source is introduced in the catheter lumen at its proximal end and pushed by use of the transfer wire to its distal end. After the predetermined treatment time, the radiation source is retracted by pulling out the transfer wire from the catheter. Alternatively, the radiation source may be engaged with the transfer wire at is distal end and may be pulled by said transfer wire to the distal end of the catheter and pushed back therefrom during retracting the same.

In case of a radiation source comprising a magnetic elongated container movement of said radiation source in steps (c) and/or (e) may be achieved by applying an external magnetic field. Alternatively the transfer wire may in this case comprise a magnet to magnetically pull the radiation source in step (c) and/or (e). In a preferred embodiment the transfer wire itself is magnetic and is magnetically linked to the elongated container.

Due to the use of a catheter having a single lumen for receipt and movement of the radiation source only, the inner diameter of said lumen can be increased as compared to catheters comprising several of such lumens. Accordingly, a larger container and thus larger seeds may be used. This allows for including higher radiation dosages in each single seed. Use of a single lumen further allows for a central arrangement of the catheter and thus of the radiation source within the vessel. Thereby uniform and homogeneous radiation of the surrounding tissue is achieved. Due to the seeds being comprised in a single flexible elongated container, no gaps in the irradiated field occur and thus the radiation source needs not be moved during treatment i.e. no "stepping treatment" is required to obtain the homogeneous irradiation over the entire segment of the vessel to be treated. This further improves control of the treatment.

Of course the radiation source of the invention is not limited to use in treatment of restenotic sites, but may also be used in treatment eg. of cancer by way of irradiating the same internally.

Although being described with respect to the preferred embodiments above, this description is not to be considered limiting and the skilled worker will appreciate the possibility of several variations of the invention as defined in the appending claims, without departing from the scope of this invention.

CLAIMS

1. Radiation source for use in endovascular radiation treatment which comprises one or more treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element,
wherein said seeds are comprised in an elongated container having at least one deflection site.

2. Radiation source of claim 1, wherein the elongated container is a hollow cylinder.

3. Radiation source of claims 1 and 2, wherein the container is made from a highly flexible material, preferably a Ni-Ti-alloy or aluminum alloy, more preferably Nitinol or Tinal alloy BB.

4. Radiation source of claims 1 to 3, wherein the one or more deflection site(s) comprise perforation patterns, preferably laser perforations of the container.

5. Radiation source of claims 1 to 4, wherein the one or more deflection site(s) comprise multiple helical openings in the tube.

6. Radiation source of claims 1 to 5, wherein the seeds comprise rounded or spherical end caps on one or both ends.

7. Radiation source of claims 1 to 6, wherein the seeds are separated from each other by at least one spacer, preferably in form of a sphere.

8. Radiation source of claims 1 to 5, wherein the seeds are spaced from each other and fixed to the inner wall of the container.

9. Radiation source of claims 1 to 8, wherein said means for containment is a metallic capsule.

10. Radiation source of claim 1 to 9, wherein the radiation emitting element comprises any α-, β- and/or γ-emitting substance.

11. Radiation source of claim 10, wherein the radiation emitting element comprises one or more radioactive materials selected from the group consisting of Cs^{137}, Co^{57}, Sr^{89}, Y^{90}, Au^{198}, Pd^{103}, Se^{75}, Sr^{90}, Ru^{106}, P^{32}, Ir^{192}, Re^{188}, W^{188} and I^{125}.

12. Apparatus for endovascular radiation treatment, comprising an elongated catheter having a proximal end portion, a distal end portion and a single lumen for receiving a radiation source, optionally a guide wire and a second lumen therefore, and a radiation source which comprises one or more treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element,
wherein said seeds are comprised within an elongated container having at least one deflection site.

13. Apparatus of claim 12, wherein a radiation source according to claims 1 to 11 is used.

14. Apparatus of claims 12 or 13, further comprising a containment vessel for radiation protection.

15. Apparatus of claims 12 to 14, further comprising a magnetic means.

16. Apparatus of claims 12 to 15, further comprising a x-ray fluoroscopy device.

17. Method for endovascular radiation treatment comprising the steps of

(a) directing an elongated catheter, having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation

source, to the selected site to be treated preferable by way of a guide wire in a separate lumen,

(b) introducing a radiation source into the catheter at its proximal end portion, which radiation source comprises one or more treating elements (seeds), wherein said seeds are comprised in an elongated container having at least one deflection site.

(c) moving said radiation source to said distal end portion preferably by way of a transfer wire;

(d) maintaining said radiation source at said distal end portion for a determined period of time, and

(e) retracting said radiation source to the proximal end portion preferably by use of a transfer wire.

18. Method of claim 17, wherein moving and/or retracting in steps (c) and/or (e) is achieved by pushing or pulling the radiation source.

19. Method of claims 17 and 18, wherein said movement in step (c) is achieved by pushing and said movement in step (e) is achieved by pulling said radiation source.

20. Method of claims 17 to 19, wherein the radiation source is linked to a transfer wire at its proximal end and moving in step (c) occurs by pushing the transfer wire into the catheter and retracting in step (e) occurs by pulling the transfer wire out of the catheter.

21. Method of claims 17 to 20, wherein a radiation source comprising a magnetic elongated container is used and movement in steps (c) and/or (e) is achieved by magnetically pushing and/or pulling the radiation source using a transfer wire comprising a magnet or using an external magnetic means.

22. Method of claims 17 to 21, wherein a radiation source according to one of claims 1 to 11 is used.

Fig. 1a

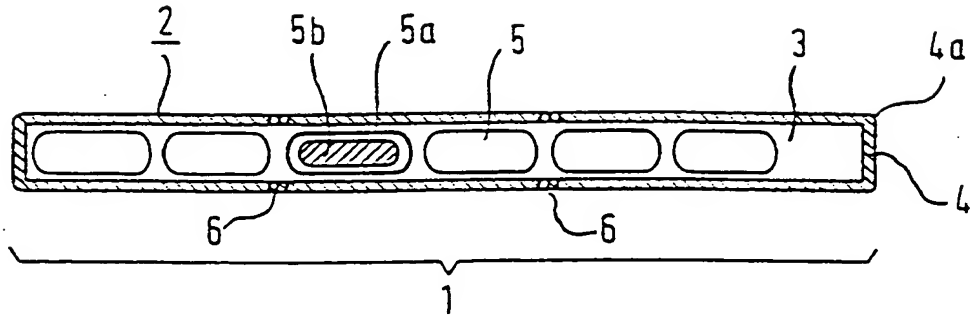


Fig. 1b

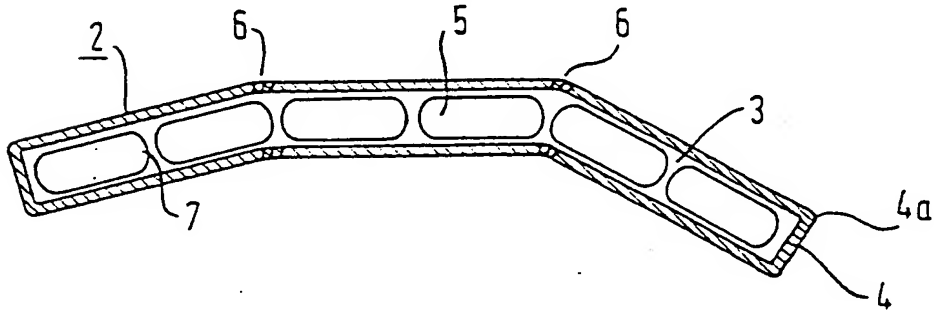


Fig. 1c

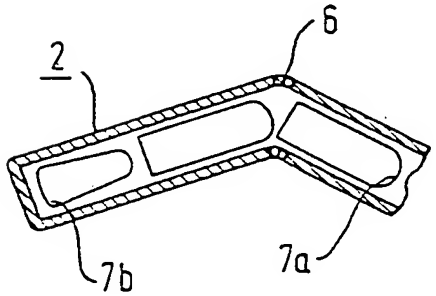


Fig. 2

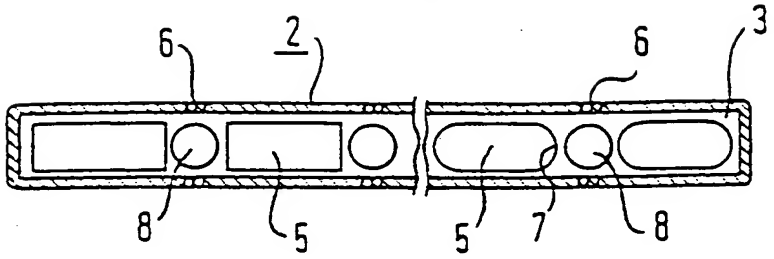


Fig. 4

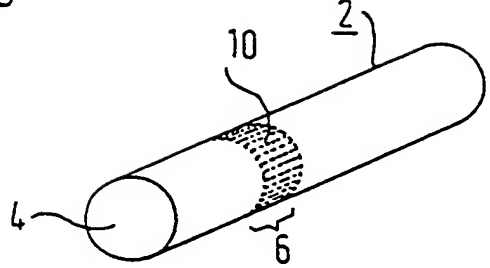


Fig. 3

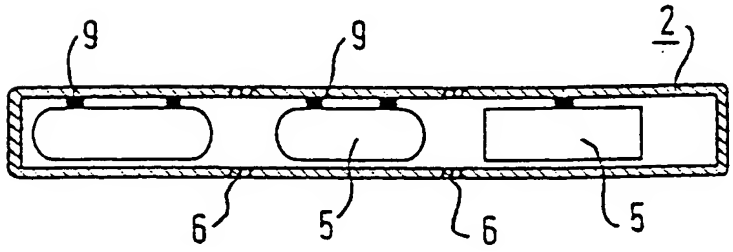


Fig. 5

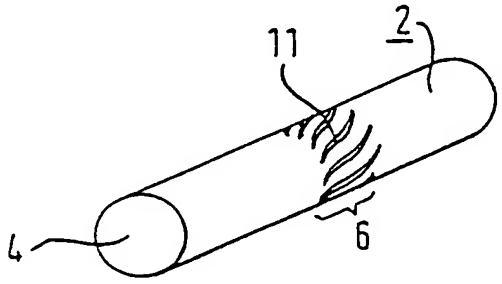
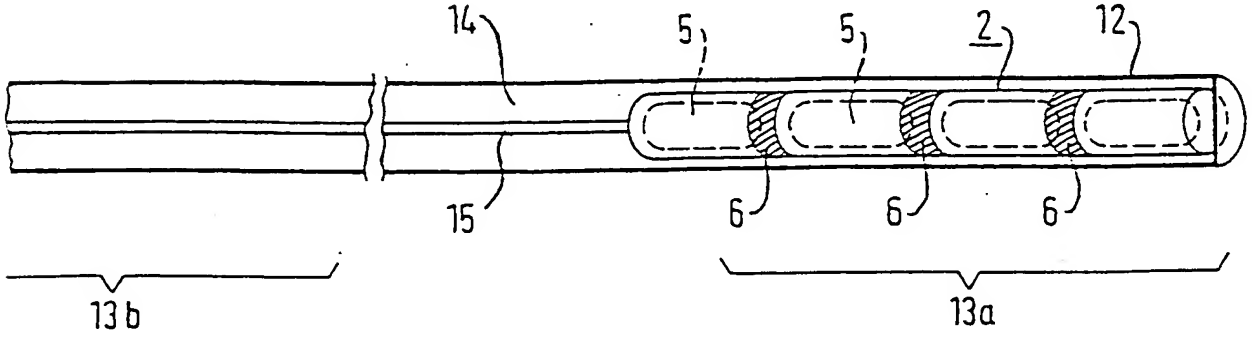


Fig. 6



INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/EP 00/05632

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N G21G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 18012 A (LOCALMED INC) 22 May 1997 (1997-05-22) page 24, line 3 - line 5 page 27, line 37 -page 28, line 3 page 35, line 36 -page 37, line 17; figures 36A,37A page 41, line 21 - line 31	1-3,6,7, 10-14,16
X	US 5 833 593 A (LIPRIE SAM F) 10 November 1998 (1998-11-10) cited in the application column 7, line 12 -column 9, line 8 column 10, line 16 - line 36 column 11, line 13 - line 56	1-3,6, 9-13,16
A	US 5 199 939 A (DAKE MICHAEL D ET AL) 6 April 1993 (1993-04-06) column 5, line 18 - line 50	1,7

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 September 2000	02/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Petter, E

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 00/05632

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 281 869 C (BRIEDE OTTO) 3 February 1915 (1915-02-03) the whole document	12,15
P,X	EP 0 993 843 A (TERUMO CORP) 19 April 2000 (2000-04-19) column 5, line 57 -column 6, line 9 column 7, line 39 -column 8, line 16 column 12, line 55 -column 13, line 23; figure 8 column 14, line 21 - line 31; figure 10	1-16

INTERNATIONAL SEARCH REPORT

information on patent family members

Intr ional Application No
PCT/EP 00/05632

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9718012 A	22-05-1997	US 5840008 A	24-11-1998
		US 5863284 A	26-01-1999
		AU 7525596 A	05-06-1997
		EP 0956096 A	17-11-1999
US 5833593 A	10-11-1998	AU 7665696 A	29-05-1997
		EP 0873157 A	28-10-1998
		JP 2000500040 T	11-01-2000
		WO 9717104 A	15-05-1997
US 5199939 A	06-04-1993	NONE	
DE 281869 C		NONE	
EP 0993843 A	19-04-2000	JP 2000116802 A	25-04-2000
		JP 2000126317 A	09-05-2000

RADIATION SOURCE FOR ENDOVASCULAR RADIATION TREATMENT

[0001] The present invention relates to a radiation source for use in endovascular radiation treatment which radiation source comprises radiation emitting elements and is suitable for being delivered in a catheter to the selected site to be treated within the vascular system of a patient. The invention further relates to an apparatus for vascular radiation treatment using said radiation source as well as a method of treatment.

BACKGROUND OF THE INVENTION

[0002] Endovascular radiation treatment is the todays method of choice to prevent formation of scar tissue in a blood vessel which has been injured in various ways, for example, as trauma from surgical or diagnostic procedures. One area of the vascular system of particular concerns with respect to such injury is coronary arteries that are subjected to procedures for removing or reducing blockages due to plaque within the arteries. Partial and even complete blockage of the coronary arteries by the formation of an arteriosclerotic plaque is well known and a serious medical problem. Such blockages may be treated using arterectomy devices which mechanically remove the plaque, hot or cold lasers which vaporize the plaque, stents which hold the artery open and other devices and procedures well known in the art. The most common of them is the percutaneous transluminal coronary angioplasty, more commonly referred to as balloon angioplasty.

[0003] In this procedure a catheter having an inflatable balloon at its distal end is introduced into the coronary artery, the uninflated balloon is positioned at a stenotic site and the balloon is inflated. Inflation of the balloon disrupts and flattens the plaque against the arterial wall and stretches the arterial wall, resulting in enlargement of the intraluminal passageway and increased bloodflow. After such extension, the balloon is deflated and the balloon catheter removed.

[0004] Long term success of balloon angioplasty procedures is largely limited due to restenosis or re-closing of the intraluminal passageway through the artery by formation of scar tissue.

Restenosis is experienced in approximately 30 to 50% of the patients within six months after balloon angioplasty. Apparently restenosis is to a significant extend a natural healing response to the vessel injury caused by inflation of the angioplasty balloon.

[0005] Such injury of the vessel typically initiates the bodies own natural repair and healing process. During the healing process, fibrin and plathelets rapidly accumulate in the endothelium and vascular smooth muscle cells proliferate and migrate into the intima. The formation of scar tissue by smooth muscle proliferation (hyperplasia) is believed to be a major contributor to restenosis following balloon angioplasty of the coronary artery.

[0006] Prior attempts to inhibit restenosis have included the use of various light therapies, chemotherapeutical agents, stents, arterectomy devices, hot and cold lasers and so on. The most promising approach to inhibit restenosis is the use of endovascular radiation therapy, i.e. the exposure of the restenotic site to ionizing or radioactive radiation.

[0007] Although endovascular radiation therapy in general has been applied advantageously, the devices available for delivery of radiation sources and the radiation sources themselves have certain drawbacks which limit their usefulness. Typically, the devices include a catheter, which is directed by way of a guide wire inserted therein to the site of treatment. The catheter is then used to internally direct the radiation source to the site of treatment.

[0008] One typical problem encountered with the catheter and/or the radiation source is related to stiffness of the source which is mostly directly proportional to its length. Thus shorter radiation sources are typically used to allow them to follow the bends of the artery. To irradiate the entire site of the vessel to be treated a so-called "stepping-treatment" is then employed, wherein the radiation source is moved back and forth in the vessel. Since, however, exact positioning is not possible in a constantly moving vessel, irradiation is not precisely controllable in this "stepping-

treatment". Thus, long sources are desirable which allow for one-step treatment of the site in its entire length.

[0009] For example, US-A-5,833,593 discloses a flexible source wire which is modified at its treatment end to receive a radioactive element. A plug seals the unmodified section of the source from the lumen of the modified segment or container which contains the radioactive element. Both ends of the source wire are sealed to prevent leakage of radioactivity. The source wire is then inserted in a catheter for guiding the same to the treatment site. The modified section or container itself is rigid and is only flexibly linked to the remainder, unmodified portion of the source.

[00010] From US-A-5,683,345 an apparatus and a method are known which apparatus includes an elongated flexible catheter tube having proximal and distal end portions with one or more lumina extending therebetween. One or more treating elements or seeds containing radioactive material are positionable within the first lumen and are movable between the proximal and distal end portions under the force of liquid flowing through the lumina. The radiation source used according this document consists of individual treating elements which may be joined together to form a train of treating elements by use of several length of high tempered spring wire to prevent the treating elements from becoming too spaced apart while moving through the catheter.

[00011] Other typical drawbacks encountered with prior art radiation sources and devices for delivering the same to the site to be treated are related to the duration of exposure, controllability of the radiation exposure (dosage, homogeneity of treatment), the necessity to conduct a "stepping-treatment", or difficulties in completely and controllably retracting the radiation source from the catheter and therefore the risk of undesirable exposure of both the patient and any medical personal handling the treatment device. It is the object of the invention to overcome these and other drawbacks of prior art radiation sources.

SUMMARY OF THE INVENTION

[00012] In a first aspect the invention relates to a radiation source for use in endovascular radiation treatment which comprises one or more, preferably at least two treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element, wherein said seeds are comprised in an elongated container having at least one deflection site.

[00013] According to a preferred embodiment the elongated container is made from a highly flexible material such as plastics, rubber, or a memory resistant material such as a Ni-Ti-alloy or an aluminum alloy, more preferably Nitinol or Tinal alloy BB.

[00014] According to a preferred embodiment, the elongated container is a hollow cylinder or tube preferably having end caps or plugs to close the same. Preferably these end caps are rounded end caps to allow for easy movement of the container.

[00015] Preferably the one or more deflection site(s) comprise perforation patterns, preferably laser perforations of the container. These perforations may be arranged in a belt around the same. The one or more deflection site(s) may also comprise multiple helical openings in the container, which as well may be arranged in a belt around the elongated container.

[00016] Preferably the seeds comprise spherical or rounded end caps on one or both ends. They may be separated from each other by interdisposing at least one spacer, preferably in form of a sphere therebetween.

[00017] According to another embodiment the seeds are spaced from each other and fixed to the inner wall of the container, preferably by way of point welding.

[00018] In another aspect the invention relates to an apparatus for endovascular radiation treatment, comprising (1) an elongated catheter having a proximal end portion and a distal end portion, a lumen extending therebetween for receiving a radiation source, (2) optionally a guide wire and a second lumen therefore, and (3) a radiation source which comprises one or more and preferably at least two treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element, wherein said seeds are comprised within an elongated container having at least one deflection site.

[00019] Preferably the apparatus comprises a x-ray fluoroscopy device for monitoring the radiation source.

[00020] In another embodiment the apparatus may comprise a magnetic means for guiding the radiation source. In this case the elongated container is preferably made from a magnetic material such as Fe or an Fe-alloy.

[00021] Preferably the apparatus may also comprise a containment vessel for storage of the elongated container and/or the individual seeds. The containment vessel can be in flow communication with the catheter lumen and/or can be a separate or separable device for separate storage and/or disposal.

[00022] In a preferred embodiment the container is linked to a transfer wire for moving the same in a catheter. Such linkage may be flexible or rigid and is preferably made at the proximal end portion of the elongated container. The transfer wire may also comprise an extension of the container itself.

[00023] In a third aspect the invention relates to a method for endovascular radiation treatment, comprising the steps of

(a) directing an elongated catheter having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, to the selected site to be treated preferably by way of a guide wire in a separate lumen,

(b) introducing a radiation source into the catheter at its proximal end portion, which radiation source comprises one or more, preferably at least two treating elements (seeds) and - wherein said seeds are comprised within an elongated container having at least one deflection site,

(c) moving said radiation source to said distal end portion of the catheter preferably by use of a transfer wire,

(d) maintaining said radiation source at said distal end portion for a determined period of time, and

(e) retracting said radiation source to the distal end portion preferably by use of a transfer wire.

[00024] Preferably moving and/or retracting in steps of (c) and/or (e) is achieved by pushing or pulling the radiation source. According to a preferred embodiment the seeds are comprised in a magnetic elongated container and the transfer wire comprises a magnet to magnetically effect said pulling of the radiation source in steps (c) and/or (e), more preferably the transfer wire itself is magnetic.

[00025] In an alternative embodiment an external magnet field may be applied to move the radiation source comprising the seeds within a magnetic elongated container by magnetic forces.

[00026] According to another embodiment movement in step (c) is achieved by pushing and movement in step (e) is achieved by pulling the elongated container using a transfer wire linked to the container at its proximal end portion.

SHORT DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic view of the radiation source according to the invention in straight (Fig. 1a) and bent (Fig. 1 b) position, Fig. 1c showing various forms of the seeds to be used.

Fig. 2 is a schematic drawing of a radiation source according to the invention comprising spheres as spacers between the seeds to form internal joints.

Fig. 3 is a schematic drawing of a radiation source according to the invention, wherein the seeds are spaced apart from each other and are fixed to the inner wall of the container by point welding.

Fig. 4 is a schematic drawing of a radiation source according to the invention wherein the deflection site of the container is formed e.g. by laser perforations.

Fig. 5 is a schematic drawing of the container according to the present invention, wherein the deflection site is formed by helical openings in the container.

Fig. 6 is a schematic drawing of the catheter of the present invention.

[00027] In the above figures like reference numerals indicate like parts of the radiation source.

DETAILED DISCLOSURE OF THE INVENTION

[00028] In the following the invention will more in detail be disclosed and illustrated by way of reference to accompanying drawings. Radiation in the sense of the application is to be understood as ionizing or radioactive radiation.

[00029] The radiation source for use in endovascular radiation treatment according to the invention comprises one or more, preferably at least two treating elements, so-called seeds. These seeds comprise a radiation emitting element or radiation emitting core and a means for containment of said radiation emitting element. The radiation source of the invention is characterized in that the seeds are comprised in an elongated container having at least one deflection site. Held together in the container the seeds form an elongated flexible radiation source of the desired length which length is determined by the length of the container chosen.

The expression "container" relates to any means capable of receiving and holding together the seeds, although the seeds need not necessarily be directly attached or linked to each other.

[00030] The expression "deflection site" refers to a site at which at least one deflection part of the elongated container can be made to deviate from the longitudinal axis thereof, typically by bending the same. Bending may be accomplished by some type of joint, formed internally or externally, or merely due to flexibility of the container material itself.

[00031] The expression "elongated" is used herein to indicate that the container has longitudinal axis larger than its height or depth. It is to be understood that the shape of the container can be chosen freely provided it meets the above requirement of being "elongated" and further provided its shape does not interfere with its movement in a catheter. Typically the container will thus have a circular cross-section, but may also have cross-sections of irregular, elliptic, rectangular, hexagonal, octagonal etc. form.

[00032] Preferably the container is in form of a hollow cylinder or tube preferably having end-plugs or end caps, preferably rounded (no sharp edges), at both ends to close the same. However, the container needs not necessarily be tightly closed, but may be comprised of a mesh, or a woven or non-woven material, provided this material allows to hold the seeds together within the form of the container and equally allows for providing deflection sites therein.

[00033] The container may be made from any suitable material which is sufficiently resistant against irradiation, permits transmission of radiation therethrough and allows for formation of deflection sites. Preferably the container is made from a flexible material such as plastics, thermoplastic resins, acrylics, rubber or from a memory-resistant material such as Ni-Ti-alloys e.g. Nitinol or aluminum alloys such as Tinal alloy BB. In a preferred embodiment the container is a hollow cylinder made of Nitinol and comprises rounded end caps made from the same material.

[00034] According to another embodiment the container may be made from or may comprise a metallic material which may either be a magnetic or a magnetizable material such as steel, stainless steel, Co, Ni, Fe, Mn, ferrites Ag, Pb, Co, Cr, Nb or their alloys, which magnetizable material can be magnetized by applying an external magnetic field.

[00035] The elongated container may comprise a coating layer which allows for reducing friction to improve movement of the elongated container within the catheter. This coating may be for example of teflon material or a similar low-friction material to reduce friction between the elongated container and the internal wall of the catheter in which it moves.

[00036] In case the container is made from a flexible material itself or from a mesh, a woven or non-woven web, deflection sites are constituted by appropriate choice of material of the container.

[00037] According to a preferred embodiment, the one or more deflection site(s) comprise perforation patterns, preferably laser perforations of the elongated container which are preferably

arranged in a belt around the container at an appropriate site to form a deflection site. The one or more deflection site(s) may equally comprise multiple helical openings in the container. These are again arranged appropriately in a belt around the container at the suitable site.

[00038] Preferably the one or more deflection sites are arranged such that each is located exactly over the portion of the internal lumen of the container, where two end caps of seeds are opposingly faced to each other.

[00039] In a preferred embodiment the seeds comprise rounded, preferably spherical end caps on one or both sides thereof. These rounded or spherical end caps may function as internal joints. According to another embodiment the seeds are separated from each other by at least one spacer, preferably in form of a sphere preferably having about the same diameter as the seeds. This sphere may function as an internal joint. In this embodiment the seeds need not necessarily comprise rounded or spherical end caps, but may have flat end caps as well. The seeds may be spaced apart by two or more spheres interdispersed therebetween, but preferably are separated by only one sphere. The spacer itself is limited with its diameter by the internal diameter of the container and may have a smaller diameter than the seeds, provided it still sufficiently functions as an internal joint.

[00040] According to another embodiment the seeds are spaced apart from each other and are fixed to the internal wall of the elongated container to held them spaced apart and to thereby allow for providing an internal deflection site of the container. Preferably fixing of the seeds is made by point welding.

[00041] The internal diameter of the container must be sufficient to slidably receive the seeds with their means for containment typically having an outer diameter of between 0.2 and 0.8 mm. As regards the longitudinal dimension, i.e. the internal length of the lumen of the elongated container, this must be sufficient to receive the one or more, preferably at least two seeds and is

preferably sufficient to receive a sufficient number of seeds to provide a radiation source of the desired length.

[00042] The internal lumen of the container may be evacuated, may comprise a gas or may comprise any suitable liquid, such as sterilized water, phosphate buffered saline, a saline solution, any inert hydrocarbon etc. provided its filling does not interfere with radiation treatment.

[00043] The outer diameter of the elongated container is as to the lower limit limited by the internal diameter thereof and is on the other hand small enough to slidably fit in a catheter and a blood vessel to be treated. Preferably such diameter is in the range of above about 0.3 to about 1 mm.

[00044] The radiation source of the present invention comprises one or more, preferably at least two treating elements or seeds. Typically the number of seeds comprised in this radiation source is chosen to cover the desired length of the vessel to be treated. Preferably the radiation source will cover a number of seeds sufficient to provide a radiation source of at least 4 mm in length, preferably 10 to 50 mm in length, more preferably 20 to 40 mm in length. The length of the elongated container is chosen appropriate thereto.

[00045] Typically the individual seeds will have a length in the range of 1.0 to 10.0 mm, more preferably 1.5 to 4.0 mm and most preferred 2.0 to 3.0 mm. Preferably the seeds are of tubular shape and have an outer diameter of the means of containment thereof in the range of between 0.2 and 1.0 mm, preferably between 0.2 and 0.8 mm.

[00046] The means for containment typically is a capsule. This capsule may be elongated, and may be a hollow cylinder or tube comprising a first and a second end plug, but may have any shape suitable for forming seeds such as spheres, ellipsoids, doughnuts, cones, flat-end-tubes,

disks, cubes etc., provided it comprises a cavity for receiving and enclosing said radiation emitting element.

[00047] Preferably the means for containment is a metallic capsule which is, for example, made from a metal selected from the group comprising stainless steel, Ag, Pt, Ti, Ni, Fe, Mn, Cr, Nb, Co, Au or their alloys, including mixtures thereof. More preferably the means for containment, i.e. the seed comprises rounded or spherical end caps on one or both ends, which end caps may also form the above first and second end plug. The means for containment may also be formed from glass or plastics material such acrylics e.g. by coating a solid radiation emitting element to obtain a tight coating layer, provided it prevents leakage of radioactivity in the lumen of the catheter. It may further comprise a coating e.g. of Teflon material or a similar low-friction material to reduce friction between the treating element or seed and the inner wall of the container.

[00048] The radiation emitting element comprised in that means for containment comprises any α-, β- and/or γ-emitting substance, preferably a pure β-particle emitter or a β- and γ-emitting substance. Typically the radiation emitting element comprises one or more radioactive materials selected from the group comprising Cs^{137}, Co^{57}, Sr^{89}, Y^{90}, Au^{198}, Pd^{103}, Se^{75}, Sr^{90}, Ru^{106}, P^{32}, Ir^{192}, Re^{188}, W^{188} and I^{125}.

[00049] The radioactive material may be contained in a solid such as metal, glass, foil or ceramics or in a free flowing form such as a powder or liquid or is dispersed in a fluid. Neither form or state of the radioactive material is crucial, provided it allows for introducing the same in the means for containment and for secure containment.

[00050] The seeds are prepared by introducing the radiation emitting element into the means for containment and closing the same, e.g. by fixing the second end plug, e.g. by welding. The seeds may also be formed by coating an appropriately shaped ceramic radioactive core with a means for containment, e.g. by dipping the core in a coating solution, sputtering etc. The entire radiation

source is then prepared by introducing the desired number of seeds into the elongated container previously prepared by known techniques and closing the same, if desired.

[00051] The amount of radioactivity is typically in the range of 0.45 to 25,000 mCi per centimeter of vessel to be treated, depending on the radiation source used. The emitted radiation should be sufficient to deliver a desired dosage of from 100 to about 10,000 rads, preferably about 700 to 5,000 rads in a about 2 to 10 minutes to the tissue to be treated.

[00052] The elongated radiation source as shown in Fig. 1 comprises an elongated container (1) comprising a hollow tube (2) and flat end plugs (4) having rounded edges (4a). The internal lumen (3) of the container is adapted to receive several seeds (5) comprising a means for containment (5a) and a radiation emitting element (5b). The hollow tube of the container further comprises deflection sites (6). As can be seen from Fig. 1 and 1a, the deflection sites (6) are located at a region of the tube where internally the spherical or rounded end caps (7) of two seeds (5) are opposingly faced to each other. Thereby, the spherical end caps function as internal joints to support bending of the deflection site(s). Further, the end caps allow for homogenous three-dimensional distribution of radiation from the seed so that bending of the radiation emitting source or the container does not result in inhomogenities of irradiation of the surrounding tissue.

[00053] Fig. 1c shows various types of seeds with spherical (7a) or rounded (7b) end caps, which can be used in the radiation source of the invention.

[00054] According to another preferred embodiment as shown in Fig. 2, the individual seeds (5) as comprised within the container lumen (3) are spaced apart from each other by inter- disposed spheres (8). These spacers in the form of spheres need not comprise a radiation emitting element or core but may be constituted of a neutral, non-radiation emitting material.

[00055] As shown in Fig. 2 the seeds (5) may comprise spherical end caps (7), but may also comprise flat ends having rounded edges (rounded end caps), since the one or more sphere(s) interdisposed between the seeds sufficiently support bending of the deflection sites (6) already. Again the deflection site (6) is suitably located in a position surrounding the interdisposed sphere (8) to create optimal a match with the internal deflection site of the elongated container (1).

[00056] According to another preferred embodiment as shown in Fig. 3 the seeds (5) comprised in the container lumen (3) are fixed to the internal wall of the elongated container (2) by way of point welding. Fixing may occur at one or more sites on the means of the containment (9) of the seed. Preferably the deflection sites (6) of the container (2) are arranged such that they match the gaps between the seeds fixed to the internal container wall.

[00057] As can be seen from Fig. 4 and Fig. 5, according to these preferred embodiments each of the one or more deflection site(s) of the container in the respective embodiments is constituted by a belt surrounding its outer diameter of a perforation pattern (10) or e.g. helical openings (11).

[00058] The radiation source of the invention comprising an elongated container having at least one deflection site and seeds held together in this container provides a radiation source which is movable by pushing or pulling the entire container. Such movement may be accomplished by use of a transfer wire which can be mechanically and/or magnetically linked to one end of the elongated container.

[00059] The invention thereby simplifies handling of the radiation source and avoids distribution of the seeds within the catheter lumen by chance. At the same time the length of the source is not limited by its stiffness or rigidity due to the at least one deflection site provided in the container. Thus, the radiation source of the invention allows for an elongated source permitting a one-step radiation treatment of elongated segments of the vessel. Due to the one or more deflection site(s)

provided in the elongated container of the radiation source of this invention, the radiation source can easily follow the bends and partitions of a blood vessel within the body to be treated.

[00060] Since the radiation source of the invention can be moved by pushing and pulling the radiation source of the invention can be used in a catheter comprising only one central lumen for receiving the source and optionally the transfer wire. Accordingly, the radiation source or its seed can be arranged in the central axis of the vessel to be treated to allow for a uniform and homogenous radiation of the surrounding tissue. This has to be considered an important aspect as radiation intensity decreases strongly with distance from the radiation source and an out of center location of the radiation source will result in unpredictable and non-controllable inhomogenities in the radiation field created therefrom. Thus, with an out of center arrangement of the radiation source inhomogeneous radiation of the surrounding tissue results. This is overcome by use of the present radiation source.

[00061] According to the present invention, there is further provided an apparatus for endovascular radiation treatment comprising (1) an elongated catheter having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, (2) optionally a guide wire in a separate lumen and (3) a radiation source as disclosed above.

[00062] Referring to Fig. 6 the apparatus of the invention makes use of a catheter (12) which is typically made from nylon material although other plastic material may be used as well. The outer diameter of the catheter is sized according to the intended application, e.g. 5 mm or smaller for use in treating the stenotic site of a coronary artery. The inner diameter of the lumen (14) extending between the distal end portion (13a) and the proximal end portion (13b) of the catheter is correspondingly sized to receive the elongated container and is typically in the range of from about 0.3 to about 1.0 mm. The catheter may not have sufficient strength or torsional rigidity for insertion along a lengthy serpentine vascular path and may then require use of a guide wire. This guide wire is then arranged in a separate lumen having in most cases a smaller diameter than the

lumen for receiving the radiation source. Typically angioplasty procedures result in a distance between the percutaneous entryport and the coronary artery of approximately 90 to 120 cm, the length of the catheter corresponding thereto. The lumen may internally have a coation for to reduce friction and/or may be filled with a suitable liquid such as mentioned above for the elongated container.

[00063] To assist in positioning the distal end portion (13a) of the catheter (12) at the desired location or site to be treated, the catheter may be advanced over a guide wire (not shown) that is pre-inserted to the desired location in the manner well known in the art. The guide wire is one commonly used in prior art and can be made from any type of metal, preferably memory-resistant metals, i.e. materials that can accept up to a 1 % strain with less than a 1 % permanent alteration in its original configuration. Preferred materials include nickel-titanium alloys such as Nitinol or aluminum alloys such as Tinal alloy BB. In the apparatus of the invention, a separate wire as above, the so-called transfer wire (16), is used for moving said radiation source. In the terms of the description a guide wire is used for directing the catheter, whereas a transfer wire is used for moving the radiation source.

[00064] The apparatus of the invention may further comprise a containment vessel for a storage of the radiation source and for shielding the patient to be treated and the medical personal from exposure from radiation during introduction and retraction of the catheter. The containment vessel preferably is in flow communication with the catheter, although it can be constructed as a separate and/or separable part to allow for separate storage and disposal.

[00065] The apparatus of the invention may further comprise a x-ray fluoroscopy device for monitoring the radiation source as, for example, described in US-A-5,833,593. This allows for exact positioning of the radiation source, which may in this case carry a marker on one or both ends, and thus allows for precise control of the treatment site.

[00066] Finally, the apparatus of the invention may comprise a magnetic means for guiding the radiation source in case the radiation source is created from a magnetic container.

[00067] In a third aspect there is provided a method for vascular radiation treatment comprising the steps of

(a) directing an elongated catheter having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, to the selected site to be treated preferably by way of a guide wire in a separate lumen,
(b) introducing a radiation source into the catheter at its proximal end portion, which radiation source comprises one or more, preferably at least two treating elements (seeds), said seeds comprising a radiation emitting element and means for containment of said radiation emitting element, and said seeds being comprised in an elongated container having at least one deflection site,
(c) moving said radiation source to said distal end portion preferably by use of a transfer wire,
(d) maintaining said radiation source at said distal end for a determined period of time, and
(e) retracting said radiation source to the proximal end portion preferably by use of a transfer wire.

[00068] Preferably a radiation source as above is used. The steps of moving and/or retracting (c) and/or (e) can be achieved by pushing or pulling the radiation source.

[00069] More in detail, according to one preferred embodiment, movement in step (c) is achieved by pushing and said movement or retracting in step (e) is achieved by pulling said radiation source. For doing so, the radiation source may be mechanically and/or magnetically linked to a transfer wire at its proximal end. In this embodiment the radiation source is introduced in the catheter lumen at its proximal end and pushed by use of the transfer wire to its distal end. After the predetermined treatment time, the radiation source is retracted by pulling out the transfer wire

from the catheter. Alternatively, the radiation source may be engaged with the transfer wire at is distal end and may be pulled by said transfer wire to the distal end of the catheter and pushed back therefrom during retracting the same.

[00070] In case of a radiation source comprising a magnetic elongated container movement of said radiation source in steps (c) and/or (e) may be achieved by applying an external magnetic field. Alternatively the transfer wire may in this case comprise a magnet to magnetically pull the radiation source in step (c) and/or (e). In a preferred embodiment the transfer wire itself is magnetic and is magnetically linked to the elongated container.

[00071] Due to the use of a catheter having a single lumen for receipt and movement of the radiation source only, the inner diameter of said lumen can be increased as compared to catheters comprising several of such lumens. Accordingly, a larger container and thus larger seeds may be used. This allows for including higher radiation dosages in each single seed. Use of a single lumen further allows for a central arrangement of the catheter and thus of the radiation source within the vessel. Thereby uniform and homogeneous radiation of the surrounding tissue is achieved. Due to the seeds being comprised in a single flexible elongated container, no gaps in the irradiated field occur and thus the radiation source needs not be moved during treatment i.e. no "stepping treatment" is required to obtain the homogeneous irradiation over the entire segment of the vessel to be treated. This further improves control of the treatment.

[00072] Of course the radiation source of the invention is not limited to use in treatment of restenotic sites, but may also be used in treatment eg. of cancer by way of irradiating the same internally.

[00073] Although being described with respect to the preferred embodiments above, this description is not to be considered limiting and the skilled worker will appreciate the possibility of

several variations of the invention as defined in the appending claims, without departing from the scope of this invention.

What is Claimed is:

1. Radiation source for use in endovascular radiation treatment which comprises one or more treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element, wherein said seeds are comprised in an elongated container having at least one deflection site.

2. Radiation source of claim 1, wherein the elongated container is a hollow cylinder.

3. Radiation source of claims 1 and 2, wherein the container is made from a highly flexible material, preferably a Ni-Ti-alloy or aluminum alloy, more preferably Nitinol or Tinal alloy BB.

4. Radiation source of claims 1 to 3, wherein the one or more deflection site(s) comprise perforation patterns, preferably laser perforations of the container.

5. Radiation source of claims 1 to 4, wherein the one or more deflection site(s) comprise multiple helical openings in the tube.

6. Radiation source of claims 1 to 5, wherein the seeds comprise rounded or spherical end caps on one or both ends.

7. Radiation source of claims 1 to 6, wherein the seeds are separated from each other by at least one spacer, preferably in form of a sphere.

8. Radiation source of claims 1 to 5, wherein the seeds are spaced from each other and fixed to the inner wall of the container.

9. Radiation source of claims 1 to 8, wherein said means for containment is a metallic capsule.

10. Radiation source of claim 1 to 9, wherein the radiation emitting element comprises any α-, β- and/or γ-emitting substance.

11. Radiation source of claim 10, wherein the radiation emitting element comprises one or more radioactive materials selected from the group consisting of Cs^{137}, Co^{57}, Sr^{89}, Y^{90}, Au^{198}, Pd^{103}, Se^{75}, Sr^{90}, Ru^{106}, P^{32}, Ir^{192}, Re^{188}, W^{188} and I^{125}.

12. Apparatus for endovascular radiation treatment, comprising an elongated catheter having a proximal end portion, a distal end portion and a single lumen for receiving a radiation source, optionally a guide wire and a second lumen therefore, and a radiation source which comprises one or more treating elements (seeds) comprising a radiation emitting element and means for containment of said radiation emitting element,
wherein said seeds are comprised within an elongated container having at least one deflection site.

13. Apparatus of claim 12, wherein a radiation source according to claims 1 to 11 is used.

14. Apparatus of claims 12 or 13, further comprising a containment vessel for radiation protection.

15. Apparatus of claims 12 to 14, further comprising a magnetic means.

16. Apparatus of claims 12 to 15, further comprising a x-ray fluoroscopy device.

17. Method for endovascular radiation treatment comprising the steps of

(a) directing an elongated catheter, having a proximal end portion, a distal end portion and a lumen extending therebetween for receiving a radiation source, to the selected site to be treated preferable by way of a guide wire in a separate lumen,

(b) introducing a radiation source into the catheter at its proximal end portion, which radiation source comprises one or more treating elements (seeds), wherein said seeds are comprised in an elongated container having at least one deflection site.

(c) moving said radiation source to said distal end portion preferably by way of a transfer wire,

(d) maintaining said radiation source at said distal end portion for a determined period of time, and

(e) retracting said radiation source to the proximal end portion preferably by use of a transfer wire.

18. Method of claim 17, wherein moving and/or retracting in steps (c) and/or (e) is achieved by pushing or pulling the radiation source.

19. Method of claims 17 and 18, wherein said movement in step (c) is achieved by pushing and said movement in step (e) is achieved by pulling said radiation source.

20. Method of claims 17 to 19, wherein the radiation source is linked to a transfer wire at its proximal end and moving in step (c) occurs by pushing the transfer wire into the catheter and retracting in step (e) occurs by pulling the transfer wire out of the catheter.

21. Method of claims 17 to 20, wherein a radiation source comprising a magnetic elongated container is used and movement in steps (c) and/or (e) is achieved by magnetically pushing and/or pulling the radiation source using a transfer wire comprising a magnet or using an external magnetic means.

22. Method of claims 17 to 21, wherein a radiation source according to one of claims 1 to 11 is used.

Abstract

According to the invention there is provided a radiation source for use in endovascular radiation treatment which comprises one or more and preferably at least two treating elements or seeds comprising a radiation emitting element and means for containment of said radiation emitting element which radiation source is characterized in that said seeds comprised in an elongated container having at least one deflection site. There is further provided an apparatus for endovascular radiation treatment comprising an elongated catheter, optionally a guide wire and the radiation source as defined above. According to another aspect there is provided a method for endovascular radiation treatment comprising the steps of directing an elongated catheter to the selected site to be treated, introducing a radiation source as defined above into the catheter at its proximal end portion, moving said radiation source to the distal end portion of the catheter preferably by use of a transfer wire, maintaining said radiation source at that distal end portion for a predetermined period of time and retracting said radiation source to the proximal end portion of the catheter preferably by use of a transfer wire.